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Notice of Allowability	Application No.	Applicant(s)	
	09/966,768	VAN DER KOOY ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the Paper filed 1 December 2006.
2. ☒ The allowed claim(s) is/are 1-11,13-17,20-22,33-38,41,42,47 and 56.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____. | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Robert Netter on 15 December 2006.

The application has been amended as follows:

In the claims

Claim 1 (Currently Amended): A method for differentiating one or more pluripotent mammalian embryonic stem (ES) cells comprising:

- a. culturing the mammalian ES cells at low cell density in a serum-free and feeder-layer free media comprising leukemia inhibitory factor; and
- b. allowing said mammalian ES cells to differentiate to primitive neural stem cells.

Claim 2 (Currently Amended): The method according to claim 1 for differentiating mammalian embryonic stem cells to cells with markers characteristic of neural cells comprising:

- a. culturing the mammalian embryonic stem cells in the serum free and feeder-layer free media at low cell density wherein said density is selected to minimize ES cell aggregation or embryoid body (EB) formation; and

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- b. allowing said mammalian ES cells to differentiate to primitive neural stem cells.

Claim 9 (Currently Amended): The method of claim 7 wherein the differentiating mammalian ES cells form at least one sphere colony.

Claim 14 (Currently Amended): The method of ~~claims~~ claim 1 wherein the serum free media further comprises a growth factor.

Claim 20 (Currently Amended): A method for producing secondary mammalian primitive neural stem cell colonies comprising:

- a. culturing mammalian ES cells in low cell density serum-free and feeder-layer free media comprising leukemia inhibitory factor for a time and under conditions sufficient to differentiate the said mammalian ES cells to primary primitive neural stem cell colonies;
- b. dissociating and subcloning the primary primitive neural stem cell colonies generated from the said mammalian ES cells; and
- c. administering a growth factor or survival factor to the dissociated neural cells to produce secondary primitive neural stem cell colonies.

Claim 33 (Currently Amended): A method for screening for modulators of mammalian primitive neural stem cell differentiation comprising:

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- a. culturing mammalian primitive neural stem cells in serum-free and feeder-layer free media comprising leukemia inhibitory factor under low cell density conditions in the presence of ~~the~~ a potential modulator under conditions that produce differentiation in the absence of the potential modulator;
- b. detecting any differentiation of the cells and cell types generated, if any, in the presence of the potential modulator compared to differentiation and cell types generated in the absence of the potential modulator;
- c. determining whether the potential modulator affects the differentiation of the cells.

Claim 34 (Currently Amended): A method in accordance with claim 33, wherein the potential modulators comprise any culturing conditions that may modulate cellular differentiation.

Claim 35 (Currently Amended): A method for screening for differentiation factors of cellular development comprising:

- a. culturing mammalian pluripotent embryonic stem (ES) cells in serum free media comprising leukemia inhibitory factor at low cell density in the presence of the differentiation factor;
- b. allowing the mammalian pluripotent ES cells to differentiate;
- c. detecting differentiation of the cells, if any.

Claim 41 (Currently Amended): The method of claim 1 further comprising determining whether the mammalian ES cells differentiate into a homogenous uniform cell base.

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Claim 42 (Currently Amended): The method of claim 1 further comprising determining whether the mammalian ES cells differentiate into a neural cell base.

Claim 47 (Currently Amended): A method for producing secondary mammalian primitive neural stem cell colonies comprising:

- a. culturing mammalian ES cells in low cell density serum-free and feeder-layer free media comprising leukemia inhibitory factor for a time and under conditions sufficient to differentiate the said mammalian ES cells to primary primitive neural stem cell colonies;
- b. dissociating and subcloning the primary primitive neural stem cell colonies generated from the said ES cells; and
- c. administering LIF or B27 to the dissociated primary primitive neural stem cells to produce secondary primitive neural stem cell colonies.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (<http://pair-direct.uspto.gov>) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Daniel M. Sullivan, Ph.D.

Primary Examiner

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